

AMENDMENTS TO THE CLAIMS:

Please amend claims 1, 2, 6, 10, 34, 43, 44, 137, 139, 140, 163, 164 and 169, add claim 175, and cancel claims 46, 158 and 159 without prejudice or disclaimer as follows. This listing of claims replaces all prior versions and listings of claims in the application.

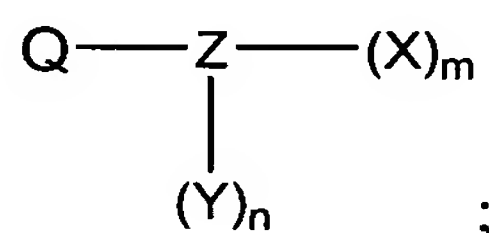
LISTING OF CLAIMS:

1. (Currently Amended) A method for identifying ~~targets and~~ non-targets of a drug, comprising:

(a) ~~contacting~~ selecting a small organic molecule drug whose non-targets with which it interacts are to be identified, and providing a capture compound that presents the drug or a fragment, intermediate, metabolite or prodrug of the drug whose non-targets are to be identified with a sample comprising biomolecules to effect capture of biomolecules in the sample, wherein:

the fragment, intermediate, metabolite or prodrug of the drug interacts with a non-target of the drug;

the capture compound has the formula:



X is a photoactivatable group that, upon exposure to light, selected to covalently binds to an amino acid side chain of a protein bind to biomolecules and requires activation following contacting with the biomolecules to effect covalent binding of the capture compound to a biomolecule protein;

Y is a the pharmaceutical small molecule organic drug or drug a fragment, drug intermediate, drug metabolite or prodrug thereof for assessing interactions with non-targets;

Q is a sorting function for immobilizing or separating the capture compounds;

Z is a trifunctional group containing 50 or fewer atoms that presents each of moiety for presenting X, Y and Q;

m is 1 an integer that is 1 to 100; and

n is an integer from 1 to 100; and

~~contacting is effected for a sufficient time for interaction between the capture compounds and the biomolecules to reach equilibrium, wherein the interaction with Y and a biomolecule reaches equilibrium;~~

(b) contacting the capture compound with a sample containing non-target proteins that interact with Y, wherein contacting is effected under conditions in which X is not activated and for a sufficient time for interaction between the capture compounds and proteins in the sample to reach equilibrium, whereby Y interacts with drug non-target proteins in the sample;

(bc) exposing the capture compound to electromagnetic radiation that activates X, whereby activating X forms to form a covalent linkage or high affinity bond between X and with protein(s) biomolecule(s) in the sample that are interacting with Y to effect capture thereof; and

(ed) isolating and identifying determining the identity of the captured biomolecules proteins, wherein the captured biomolecules identified proteins comprise drug targets and non-targets of the drug.

2. (Currently Amended) The method of claim 1, wherein ~~drug non-targets are identified~~ Z comprises an amino acid; and Q is selected from among biotin, (His)₆, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), an oligonucleotides, a nucleoside, a nucleotide, an antibody, an immunotoxin conjugate, an adhesive peptide, a lectin, a liposome, a peptide nucleic acid and an activated dextran.

3.-4. (Cancelled).

5. (Withdrawn) The method of claim 1 wherein, the moiety Y is linked to the moiety Z in different orientations via different points of attachments on the Y moiety.

6. (Currently Amended) The method of claim 1, wherein:

X is selected from among an azide or a diazarine;

Z is an amino acid; and

Q is biotin or an oligonucleotide the biomolecules are proteins.

7.-9. (Cancelled).

10. (Currently Amended) The method of claim 1, wherein following step (a) or (c), the Q permits separation of capture compounds by arraying of the capture compounds are immobilized on a solid support via Q, which binds to by binding to the surface of the support or a molecule thereon.

11.-14. (Cancelled).

15. (Previously Presented) The method of claim 1, wherein

Z is a moiety that is cleavable prior to or during mass spectrometric analysis of biomolecules bound to the capture compound.

16. (Cancelled).

17. (Withdrawn) The method of claim 1, wherein

Z is a moiety that is not cleavable prior to or during mass spectrometric analysis of biomolecules bound to the capture compound.

18. (Withdrawn) The method of claim 1, wherein:

Q is an oligonucleotide or oligonucleotide analog that includes a single-stranded portion of sufficient length "j" to form a stable hybrid with a base-complementary single stranded nucleic acid molecule or analog.

19.-21. (Cancelled).

22. (Withdrawn) The method of claim 1, wherein Q has the formula $N^1_s B_i N^2_u$, wherein:

N^1 , B and N^2 are oligonucleotides or oligonucleotide analogs comprising s, t and u members, respectively;

B is a region of sequence permutations that contains at least two bases; and sum of s, i and u is at least 5.

23. and 24. (Cancelled).

25. (Original) The method of claim 1, wherein Z is a photocleavable, acid cleavable, alkaline cleavable, oxidatively cleavable, or reductively cleavable group.

25.-33. (Cancelled).

34. (Currently Amended) The method of claim 1, wherein:

Q is selected from among biotin, (His)₆, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), an oligonucleotides, a nucleoside, a nucleotide, an antibody, an immunotoxin conjugate, an adhesive peptide, a lectin, a liposome, a peptide nucleic acid and an activated dextran; and

Z has the formula: $(S^1)_t M(R^{15})_a (S^2)_b L$, wherein:

S^1 and S^2 are spacer moieties;

t and b are each independently 0 or 1;

a is an integer from 0 to 4;

M is a central moiety possessing three or more points of attachment;

R^{15} is a monovalent group independently selected from $Y^2 R^{18}$;

Y^2 is a divalent group independently having any combination of the following groups:
a direct link, arylene, heteroarylene, cycloalkylene, $>C(R^{17})_2$, $C(R^{17})=C(R^{17})$,
 $>C=C(R^{23})(R^{24})$, $>C(R^{23})(R^{24})$, $C\equiv C$, O, $>S(A)_u$, $>P(D)_v(R^{17})$, $>P(D)_v(ER^{17})$, $>N(R^{17})$,
 $>N(COR^{17})$, $>N^+(R^{23})(R^{24})$, $>Si(R^{17})_2$ and $>C(E)$; where u is 0, 1 or 2; v is 0, 1, 2 or 3; A is O
or NR^{17} ; D is S or O; and E is S, O or NR^{17} ;

R^{17} and R^{18} are each independently selected from the group consisting of hydrogen,
halo, pseudohalo, cyano, azido, nitro, $SiR^{27}R^{28}R^{25}$, alkyl, alkenyl, alkynyl, haloalkyl,
haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl,
heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl,
hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and $NR^{19}R^{20}$;

R^{19} and R^{20} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl,
cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl and heterocyclyl;

R^{23} and R^{24} are selected from (i) or (ii) as follows:

(i) R^{23} and R^{24} are independently selected from the group consisting of hydrogen,
alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heteroaryl; or

(ii) R^{23} and R^{24} together form alkylene, alkenylene or cycloalkylene;

R^{25} , R^{27} and R^{28} are each independently a monovalent group selected from hydrogen,
alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl,
heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl,
heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy
and $NR^{19}R^{20}$;

R^{15} , R^{17} , R^{18} , R^{19} , R^{20} , R^{23} , R^{24} , R^{25} , R^{27} and R^{28} can be substituted with one or more
substituents each independently selected from Z^2 ; Z^2 is selected from alkyl, alkenyl, alkynyl,
aryl, cycloalkyl, cycloalkenyl, hydroxy, $S(O)_hR^{35}$; h is 0, 1 or 2, $NR^{35}R^{36}$, $COOR^{35}$, COR^{35} ,
 $CONR^{35}R^{36}$, $OC(O)NR^{35}R^{36}$, $N(R^{35})C(O)R^{36}$, alkoxy, aryloxy, heteroaryl, heterocyclyl,
heteroaryloxy, heterocyclyloxy, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl,
heteroaralkynyl, aralkoxy, heteroaralkoxy, alkoxycarbonyl, carbamoyl, thiocarbamoyl,
alkoxycarbonyl, carboxyaryl, halo, pseudohalo, haloalkyl and carboxamido;

R^{35} and R^{36} are each independently selected from among hydrogen, halo, pseudohalo,
cyano, azido, nitro, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkyl, alkenyl,
alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl,
heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl,

heterocyclalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy, amino, amido, alkylamino, dialkylamino, alkylaryl amino, diarylamino and arylamino; and

L is a group that is cleavable prior to or during mass spectrometric analysis of the compound.

35.-37. (Cancelled).

38. (Original) The method of claim 34, wherein L is a disulfide moiety, a photocleavable group, an acid cleavable group, an alkaline cleavable group, a oxidatively cleavable group, or a reductively cleavable group.

39.-42. (Cancelled).

43. (Currently Amended) The method of claim 1, wherein each ~~X~~ is selected from the group consisting of an active ester, an active halo moiety, an amino acid side chain-specific functional group, and a specific peptide that binds to a biomolecule surfaces M is an amino acid and S¹ and S² each is independently (CH₂)_r, where r is 1-10.

44. (Currently Amended) The method of claim 1, wherein an X is an ~~α-halo ether~~, an ~~α-halo carbonyl group~~, maleimido, a metal complex, an expoxide, and an isothiocyanate a diazirine, 3-trifluoromethyldiazirine or an azide; Z is an amino acid and Q is biotin.

45. (Cancelled).

46. (Cancelled).

47. (Withdrawn) The method of claim 1, wherein the capture compounds comprise a mass modifying tag linked to Z.

48.-54. (Cancelled).

55. (Withdrawn) The method of claim 18, wherein capture compounds are hybridized to a plurality of oligonucleotides or analogs thereof that comprise oligonucleotides that are complementary to each Q.

56. (Withdrawn) The method of claim 55, wherein the oligonucleotides or analog thereof that are complementary to Q are immobilized on a solid support as an array.

57.-62. (Cancelled).

63. (Withdrawn) The method of claim 1, wherein the Z moiety of the capture compound comprises a functionality conferring luminescence, fluorescence, chemiluminescence or colorimetric properties.

64. and 65. (Cancelled).

66. (Withdrawn) The method of claim 1, wherein the capture compounds further comprise a solubility group W that influences the solubility properties of the capture compound.

67. (Withdrawn) The method of claim 1, wherein the selectivity function Y is a drug or drug intermediate/fragment selected from among those set forth in Figure 17 and Figure 21.

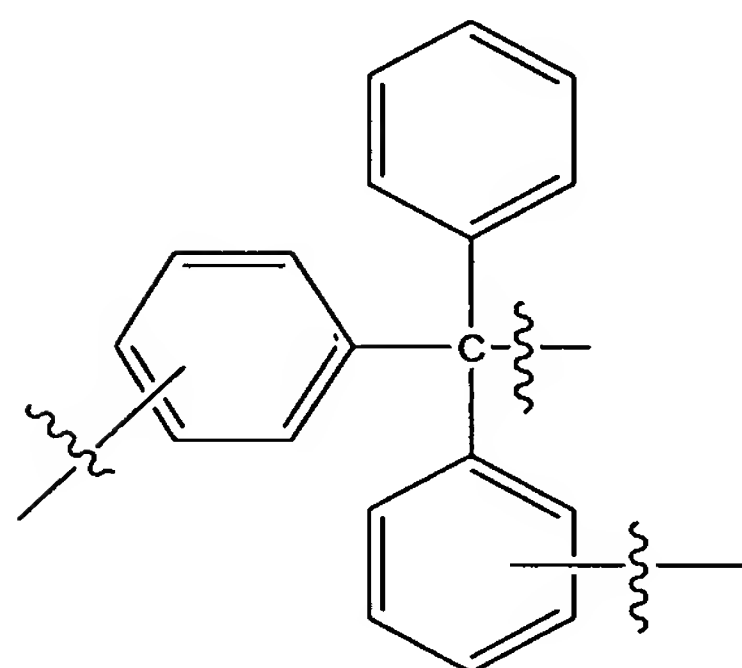
68. (Withdrawn) The method of claim 1, wherein the reactivity function X is selected from those set forth in Figure 16.

69.-74. (Cancelled).

75. (Previously Presented) The method of claim 1, wherein Q is biotin.

76. (Cancelled).

77. (Withdrawn) The method of claim 1, wherein Z has the formula:



78.-109. (Cancelled).

110. (Previously Presented) The method of claim 1, further comprising identifying or detecting a captured biomolecule by mass spectrometric analysis.

111.-115. (Cancelled).

116. (Previously Presented) The method of claim 1, wherein the sample comprises a biological sample, a body tissue or fluid or a cell lysate.

117. (Cancelled).

118.-136. (Cancelled).

137. (Currently Amended) The method of claim 1, wherein:

Q is selected from among biotin, (His)₆, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), an oligonucleotides, a nucleoside, a nucleotide, an antibody, an immunotoxin conjugate, an adhesive peptide, a lectin, a liposome, a peptide nucleic acid and an activated dextran; and

Z has the formula: $(S^1)_t M(R^{15})_a (S^2)_b$, wherein:

S^1 and S^2 are spacer moieties;

t and b are each independently 0 or 1;

a is an integer from 0 to 4;

M is a central moiety possessing three or more points of attachment;

R^{15} is a monovalent group independently selected from Y^2R^{18} ;

Y^2 is a divalent group independently having any combination of the following groups:

a direct link, arylene, heteroarylene, cycloalkylene, $>C(R^{17})_2$, $C(R^{17})=C(R^{17})$,
 $>C=C(R^{23})(R^{24})$, $>C(R^{23})(R^{24})$, $C\equiv C$, O, $>S(A)_u$, $>P(D)_v(R^{17})$, $>P(D)_v(ER^{17})$, $>N(R^{17})$,
 $>N(COR^{17})$, $>N^+(R^{23})(R^{24})$, $>Si(R^{17})_2$ and $>C(E)$; wherein:

u is 0, 1 or 2;

v is 0, 1, 2 or 3;

A is O or NR^{17} ;

D is S or O; and

E is S, O or NR^{17} ;

R^{17} and R^{18} are each independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, azido, nitro, $SiR^{27}R^{28}R^{25}$, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and $NR^{19}R^{20}$;

R^{19} and R^{20} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl and heterocyclyl;

R^{23} and R^{24} are selected from (i) or (ii) as follows:

(i) R^{23} and R^{24} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heteroaryl; or

(ii) R^{23} and R^{24} together form alkylene, alkenylene or cycloalkylene;

R^{25} , R^{27} and R^{28} are each independently a monovalent group selected from hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and $NR^{19}R^{20}$;

R^{15} , R^{17} , R^{18} , R^{19} , R^{20} , R^{23} , R^{24} , R^{25} , R^{27} and R^{28} can be substituted with one or more substituents each independently selected from Z^2 ; Z^2 is selected from alkyl, alkenyl, alkynyl,

aryl, cycloalkyl, cycloalkenyl, hydroxy, $S(O)_hR^{35}$; h is 0, 1 or 2, $NR^{35}R^{36}$, $COOR^{35}$, COR^{35} , $CONR^{35}R^{36}$, $OC(O)NR^{35}R^{36}$, $N(R^{35})C(O)R^{36}$, alkoxy, aryloxy, heteroaryl, heterocyclyl, heteroaryloxy, heterocyclyloxy, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, aralkoxy, heteroaralkoxy, alkoxycarbonyl, carbamoyl, thiocarbamoyl, alkoxycarbonyl, carboxyaryl, halo, pseudohalo, haloalkyl and carboxamido; and

R^{35} and R^{36} are each independently selected from among hydrogen, halo, pseudohalo, cyano, azido, nitro, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy, amino, amido, alkylamino, dialkylamino, alkylaryl amino, diarylamino and arylamino.

138. (Cancelled).

139. (Currently Amended) The method of claim 1 ~~137~~, wherein M is an amino acid ~~X is a photoactivatable group~~.

140. (Currently Amended) The method of claim 139, wherein ~~the capture compound interacts with the biomolecule mixture prior to activation of the photoactivatable group~~ X is an azide, S^1 and S^2 each is independently $(CH_2)_r$, where r is 1-10, and Q is biotin or an oligonucleotide.

141. and 142. (Cancelled).

143. (Withdrawn) The method of claim 1, further comprising re-designing the moiety Y to eliminate or alter its binding interactions with a captured biomolecule.

144. (Previously Presented) The method of claim 1, further comprising identifying a function of a captured biomolecule.

145. (Withdrawn) The method of claim 143, wherein the alteration in binding is an increase in binding.

146. (Withdrawn) The method of claim 143, wherein the alteration in binding is a decrease in binding.

147. (Withdrawn) The method of claim 143, wherein the biomolecule for which binding is altered is a non-target biomolecule.

148.-150. (Cancelled).

151. (Previously Presented) The method of claim 1, wherein the sample is contacted with a collection of capture compounds.

152. (Previously Presented) The method of claim 1, wherein the X moiety of the capture compound comprises an azide, diazirine or a group which, following activation, reacts with the biomolecule.

153. (Withdrawn) The method of claim 143, wherein the method is repeated with the re-designed moiety Y linked to a capture compound to effect further modification thereof.

154. (Cancelled).

155. (Withdrawn) The method of claim 143, wherein the captured biomolecule for which binding is altered is a drug target protein.

156. (Withdrawn) The method of claim 143, wherein the captured biomolecule for which binding is altered is a non-drug target protein.

157.-159.(Cancelled).

160. (Previously Presented) The method of claim 1, wherein a concentration of capture compound is varied in a plurality of different reactions.

161. (Previously Presented) The method of claim 160, wherein a dissociation constant (K_d value) is determined.

162. (Cancelled).

163. (Currently Amended) The method of claim 110, wherein the mass spectrometric analysis is performed using a mass spectrometric analysis format that is selected from among matrix assisted laser desorption ionization (MALDI), continuous or pulsed electrospray (ES) ionization, ionspray, thermospray, and massive cluster impact mass spectrometry.

164. (Currently Amended) The method of claim 163, wherein the mass spectrometric analysis ~~detection~~ format is linear time-of-flight (TOF), reflectron time-of-flight, single quadrupole, multiple quadrupole, single magnetic sector, multiple magnetic sector, Fourier transform, ion cyclotron resonance (ICR), or ion trap.

165. (Cancelled).

166. (Previously Presented) The method of claim 144, wherein the function of the biomolecule is determined by sequence alignment, pharmacophores, homology models and protein motif correlation, liver microsomes metabolic pathways, cDNA-expressed enzymes, signal pathways and back-mapping to yeast pathways, simulations and protein/protein interaction of pull-out proteins, native polymorphisms, knock-out/knock-in, flow cytometry, therapeutic activity of the drug, or prospective genotyping and prospective phenotyping.

167. (Withdrawn) The method of claim 143, wherein:

the moiety Y is a first drug; and
redesigning the first drug results in a second drug with fewer side-effects or an increased therapeutic index as compared to the first drug.

168. (Withdrawn) The method of claim 1, wherein the drug is selected from among troglitazone, rosiglitazone, pioglitazone, methotrexate, atorvastatin, celecoxib, refecoxib and cerivastatin.

169. (Currently Amended) The method of claim 1 ~~158~~, wherein the treatment comprises activation with light.

170. (Cancelled).

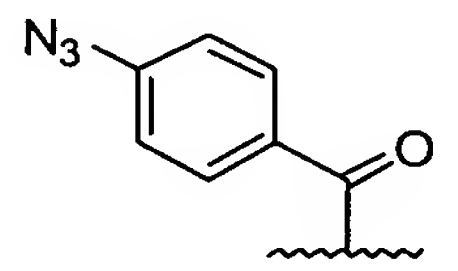
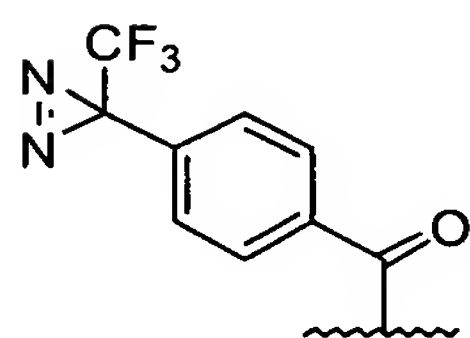
171. (Withdrawn) The method of claim 22, where B is a single stranded DNA or RNA and the number of sequence permutations is equal to 4^i , wherein i is about 2 to about 25.

172. (Withdrawn) The method of claim 171, where i is about 3 to about 5, 6, 7 or 8.

173. (Cancelled).

174. (Cancelled)

175. (New) The method of claim 1, wherein X is



or an arylazide; Z is serine, threonine, lysine, tyrosine, glutamic acid, aspartic acid or cysteine; and Q is biotin or an oligonucleotide.